



DEPARTMENT OF HEALTH & HUMAN SERVICES

m395Dn

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone: 313-226-6260

WARNING LETTER
2000-DT-25

July 6, 2000

Narendra N. Borkar, Chief Executive Officer
Caraco Pharmaceutical Laboratories, Ltd.
1150 Elijah McCoy
Detroit, Michigan 48202

Dear Mr. Borkar:

A January 18 through March 10, 2000 inspection of your firm's drug manufacturing operations found that your firm is operating in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act). During the inspection, our investigators documented numerous significant deviations from the Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Part 211), which cause your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the Act. While examples are as follows, we suggest you refer to the list of inspectional observations [the FDA-483] which was issued at the conclusion of the inspection for additional details:

1. Failure to have a quality control unit adequate to perform its functions and responsibilities, as required by 21 CFR 211.22. Your failure to have an adequate quality control unit is demonstrated by the number and types of inspectional observations made during this inspection.
2. Failure to ensure that each person engaged in the manufacture, processing, packing, or holding of a drug product has the education, training, and experience, or any combination thereof, to enable that person to perform their assigned functions, as required by 21 CFR 211.25. Your failure to have a staff with the adequate qualifications to perform their assigned functions is demonstrated by the number and types of inspectional observations made during this inspection.

3. Failure of the quality control unit to review all drug product production and control records to determine compliance with established written procedures before a batch is released or rejected, and to perform an investigation when a batch or its components fails to meet specifications, as required by 21 CFR 211.192. For examples, see FDA-483 observations 1, 2, 14, 16 and 51.
4. Failure to reject drug products failing to meet established standards or specifications and any other relevant quality control criteria, as required by 21 CFR 211.165(f). For examples, see FDA-483 observations 1, 2 and 14.
5. Failure to have, to follow, and to have a record justifying any deviations from, procedures for production and process control designed to assure that drug products have the identity, strength, quality, and purity they purport or are represented to possess, as required by 21 CFR 211.100. For example, see FDA-483 observations 2, 3, 4, 5, 6, 7, 8, 9, 16, 24, 26, 27, 29, 30, 33, 37, 38, 39 and 53.
6. Failure to make an appropriate laboratory determination of satisfactory conformance of each batch of drug product to its final specifications prior to its release, as required by 21 CFR 211.165. For example, see FDA-483 observations 2, 27 and 52.
7. Failure to have, and/or to follow, laboratory controls which include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality and purity, as required by 21 CFR 211.160. For example, see FDA-483 observations 2, 3, 13, 15, 29, 30, 31, 33, 34, 35, 36, 37, 38, 41, 42, 43, 44, 45, 46, 48, 50, 52 and 54.

8. Failure to adequately evaluate, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing and control procedures, as required by 21 CFR 211.180(e). For example, see FDA-483 observation # 9.
9. Failure to establish, and to follow, written procedures to assure that equipment has been adequately cleaned, maintained, and sanitized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond established requirements, as required by 21 CFR 211.67. For example, see FDA-483 observations 4, 18, 19, 20, 21, 22, 23, 40, 41, 42, 43 and 47.
10. Failure to assure that equipment is of appropriate design for its intended use, as required by 21 CFR 211.63. For example, see FDA-483 observations 17 and 49.
11. Failure to have and to follow written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures, as required by 21 CFR 211.80. For example, see FDA-483 observations 2, 3, 10, 34, 35, 36, 37, 38 and 53.
12. Failure to have, and to follow, a stability testing program adequate to assess the stability characteristics of drug products, as required by 21 CFR 211.166. For example, see FDA-483 observations 6, 24 and 26.

The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. In addition, we note that observations 5, 18, 19-21, 23 and 31 are repeat observations from the 5/11-6/17/99 inspection. It is your responsibility to assure adherence to each requirement of the Good Manufacturing Practice Regulations. Other Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

Page 4
Warning Letter 2000-DT-25
Caraco Pharmaceutical Laboratories, Ltd.
Detroit, MI 48202

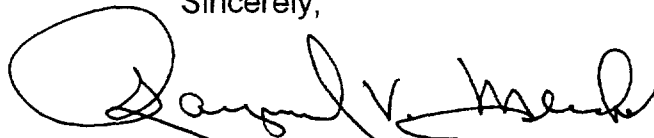
We request that you take prompt action to correct these violations. Failure to promptly correct these violations may result in enforcement action being initiated by the Food and Drug Administration without further notice, such as seizure and/or injunction.

We acknowledge receipt of your various written and verbal responses to the list of inspectional observations and your commitments to take specific steps to both correct the noted violations and to make systemic corrections to assure that similar violations will not recur. We concur in your decision to seek the assistance of outside expertise to make the necessary corrections.

Please notify this office in writing, within fifteen (15) working days of receipt of this letter, as to any additional steps you have taken to correct these violations, including an explanation of each step being taken to identify and make corrections to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be implemented.

Your reply should be directed to Sandra Williams, Compliance Officer, at the above address.

Sincerely,

A handwritten signature in black ink, appearing to read "Raymond V. Mfecko". The signature is fluid and cursive, with a large loop at the beginning and a long horizontal stroke extending to the right.

Raymond V. Mfecko
District Director
Detroit District

Enclosure:a/s

cc via certified mail: Mr. Robert Kurkiewicz, Vice President, Quality Assurance